

AP20 Rec'd PCT/PTO 23 JUN 2006

- 52 -

CLAIMS:

1. A method for preventing onset of an autoimmune disease in a subject said method comprising administering to said subject Flt-3L or a Flt-3-Flt-3L receptor agonist in an amount effective to increase a sub-type of non-activated, immature and tolerogenic DC selected from Plasmacytoid DC and CD8⁺ DC or their equivalents thereby inducing or maintaining immune tolerance in said subject.
2. The method of Claim 1 wherein the agent is Flt-3L.
3. The method of Claim 1 or 2 wherein the Flt-3L or a Flt-3-Flt-3L receptor agonist is co-administered with a cytokine.
4. The method of Claim 2 or 3 wherein the Flt-3L or a Flt-3-Flt-3L receptor agonist is co-administered with a Toll-like receptor ligand.
5. The method of Claim 3 or 4 wherein co-administration is sequential administration.
6. The method of Claim 3 or 4 wherein co-administration is simultaneous administration.
7. The method of Claim 1 wherein the subject is a human, non-human primate, livestock animal, laboratory test animal, a companion animal, a captured wild animal or an avian species.
8. The method of Claim 7 wherein the subject is a human.
9. The method of Claim 1 wherein the Flt-3L is derived from the same species to which it is administered.

- 53 -

10. The method of Claim 1 wherein the Flt-3L is derived from a different species to which it is administered.

11. The method of Claim 1 wherein the autoimmune disease is Active Chronic Hepatitis, Addison's Disease, Anti-phospholipid Syndrome, Atopic Allergy, Autoimmune Atrophic Gastritis, Achlorhydra Autoimmune, Celiac Disease, Crohns Disease, Cushings Syndrome, Dermatomyositis, Type I Diabetes, Discoid Lupus, Erythematosis, Goodpasture's Syndrome, Grave's Disease, Hashimoto's Thyroiditis, Idiopathic Adrenal Atrophy, Idiopathic Thrombocytopenia, Insulin-dependent Diabetes, Lambert-Eaton Syndrome, Lupoid Hepatitis, Lymphopenia, Mixed Connective Tissue Disease, Multiple Sclerosis, Pemphigoid, Pemphigus Vulgaris, Pernicious Anemia, Phacogenic Uveitis, Polyarteritis Nodosa, Polyglandular Auto. Syndromes, Primary Biliary Cirrhosis, Primary Sclerosing Cholangitis, Psoriasis, Raynauds, Reiter's Syndrome, Relapsing Polychondritis, Rheumatoid Arthritis, Schmidt's Syndrome, Scleroderma – CREST, Sjogren's Syndrome, Sympathetic Ophthalmia, Systemic Lupus Erythematosis, Takayasu's Arteritis, Temporal Arteritis, Thyrotoxicosis, Type B Insulin Resistance, Ulcerative Colitis and Wegener's Granulomatosis.

12. The method of Claim 11 wherein the autoimmune disease is diabetes.

13. A method of modulating the degree of tolerogenicity in a subject, or modulating the level of immune tolerance against cancer or a pathogenic agent said method comprising administering to said subject Flt-3L or Flt-3-Flt-3L receptor agonist in an amount effective to preferably increase a sub-type of non-activated, immature and tolerogenic DC selected from Plasmacytoid DC and CD8⁺ DC or their equivalents in said subject.

14. The method of Claim 13 wherein the agent is Flt-3L.

15. The method of Claim 13 or 14 wherein the Flt-3L or a Flt-3-Flt-3L receptor agonist is co-administered with a Toll-like receptor ligand.

- 54 -

16. The method of Claim 14 or 15 wherein co-administration is sequential administration.

17. The method of Claim 14 or 15 wherein co-administration is simultaneous administration.

18. The method of Claim 13 wherein the subject is a human, non-human primate, livestock animal, laboratory test animal, a companion animal, a captured wild animal or an avian species.

19. The method of Claim 18 wherein the subject is a human.

20. The method of Claim 13 wherein the Flt-3L is derived from the same species to which it is administered.

21. The method of Claim 13 wherein the Flt-3L is derived from a different species to which it is administered.

22. The method of Claim 13 in the treatment of cancer.

23. The method of Claim 22 wherein the cancer is ABL1 protooncogene, AIDS Related Cancers, Acoustic Neuroma, Acute Lymphocytic Leukaemia, Acute Myeloid Leukaemia, Adenocystic carcinoma, Adrenocortical Cancer, Agnogenic myeloid metaplasia, Alopecia, Alveolar soft-part sarcoma, Anal cancer, Angiosarcoma, Aplastic Anaemia, Astrocytoma, Ataxia-telangiectasia, Basal Cell Carcinoma (Skin), Bladder Cancer, Bone Cancers, Bowel cancer, Brain Stem Glioma, Brain and CNS Tumors, Breast Cancer, CNS Tumors, Carcinoid Tumors, Cervical Cancer, Childhood Brain Tumors, Childhood Cancer, Childhood Leukaemia, Childhood Soft Tissue Sarcoma, Chondrosarcoma, Choriocarcinoma, Chronic Lymphocytic Leukaemia, Chronic Myeloid Leukaemia, Colorectal Cancers, Cutaneous T-Cell Lymphoma, Dermatofibrosarcoma-protuberans, Desmoplastic-Small-Round-Cell-Tumor, Ductal Carcinoma, Endocrine

- 55 -

Cancers, Endometrial Cancer, Ependymoma, Esophageal Cancer, Ewing's Sarcoma, Extra-Hepatic Bile Duct Cancer, Eye Cancer, Eye: Melanoma, Retinoblastoma, Fallopian Tube cancer, Fanconi Anaemia, Fibrosarcoma, Gall Bladder Cancer, Gastric Cancer, Gastrointestinal Cancers, Gastrointestinal-Carcinoid-Tumor, Genitourinary Cancers, Germ Cell Tumors, Gestational-Trophoblastic-Disease, Glioma, Gynaecological Cancers, Haematological Malignancies, Hairy Cell Leukaemia, Head and Neck Cancer, Hepatocellular Cancer, Hereditary Breast Cancer, Histiocytosis, Hodgkin's Disease, Human Papillomavirus, Hydatidiform mole, Hypercalcemia, Hypopharynx Cancer, IntraOcular Melanoma, Islet cell cancer, Kaposi's sarcoma, Kidney Cancer, Langerhan's-Cell-Histiocytosis, Laryngeal Cancer, Leiomyosarcoma, Leukaemia, Li-Fraumeni Syndrome, Lip Cancer, Liposarcoma, Liver Cancer, Lung Cancer, Lymphedema, Lymphoma, Hodgkin's Lymphoma, Non-Hodgkin's Lymphoma, Male Breast Cancer, Malignant-Rhabdoid-Tumor-of-Kidney, Medulloblastoma, Melanoma, Merkel Cell Cancer, Mesothelioma, Metastatic Cancer, Mouth Cancer, Multiple Endocrine Neoplasia, Mycosis Fungoides, Myelodysplastic Syndromes, Myeloma, Myeloproliferative Disorders, Nasal Cancer, Nasopharyngeal Cancer, Nephroblastoma, Neuroblastoma, Neurofibromatosis, Nijmegen Breakage Syndrome, Non-Melanoma Skin Cancer, Non-Small-Cell-Lung-Cancer-(NSCLC), Ocular Cancers, Oesophageal Cancer, Oral cavity Cancer, Oropharynx Cancer, Osteosarcoma, Ostomy Ovarian Cancer, Pancreas Cancer, Paranasal Cancer, Parathyroid Cancer, Parotid Gland Cancer, Penile Cancer, Peripheral-Neuroectodermal-Tumors, Pituitary Cancer, Polycythemia vera, Prostate Cancer, Rare-cancers-and-associated-disorders, Renal Cell Carcinoma, Retinoblastoma, Rhabdomyosarcoma, Rothmund-Thomson Syndrome, Salivary Gland Cancer, Sarcoma, Schwannoma, Sezary syndrome, Skin Cancer, Small Cell Lung Cancer (SCLC), Small Intestine Cancer, Soft Tissue Sarcoma, Spinal Cord Tumors, Squamous-Cell-Carcinoma-(skin), Stomach Cancer, Synovial sarcoma, Testicular Cancer, Thymus Cancer, Thyroid Cancer, Transitional-Cell-Cancer-(bladder), Transitional-Cell-Cancer-(renal-pelvis/-ureter), Trophoblastic Cancer, Urethral Cancer, Urinary System Cancer, Uroplakins, Uterine sarcoma, Uterus Cancer, Vaginal Cancer, Vulva Cancer, Waldenstrom's-Macroglobulinemia, Wilms' Tumor.

- 56 -

24. The method of Claim 22 in the prophylaxis of a pathogenic agent-induced autoimmune disease.

25. The method of Claim 24 wherein the autoimmune disease is Active Chronic Hepatitis, Addison's Disease, Anti-phospholipid Syndrome, Atopic Allergy, Autoimmune Atrophic Gastritis, Achlorhydra Autoimmune, Celiac Disease, Crohns Disease, Cushings Syndrome, Dermatomyositis, Type I Diabetes, Discoid Lupus, Erythematosis, Goodpasture's Syndrome, Grave's Disease, Hashimoto's Thyroiditis, Idiopathic Adrenal Atrophy, Idiopathic Thrombocytopenia, Insulin-dependent Diabetes, Lambert-Eaton Syndrome, Lupoid Hepatitis, Lymphopenia, Mixed Connective Tissue Disease, Multiple Sclerosis, Pemphigoid, Pemphigus Vulgaris, Pernicious Anema, Phacogenic Uveitis, Polyarteritis Nodosa, Polyglandular Auto. Syndromes, Primary Biliary Cirrhosis, Primary Sclerosing Cholangitis, Psoriasis, Raynauds, Reiter's Syndrome, Relapsing Polychondritis, Rheumatoid Arthritis, Schmidt's Syndrome, Scleroderma – CREST, Sjogren's Syndrome, Sympathetic Ophthalmia, Systemic Lupus Erythematosis, Takayasu's Arteritis, Temporal Arteritis, Thyrotoxicosis, Type B Insulin Resistance, Ulcerative Colitis and Wegener's Granulomatosis.

26. The method of Claim 25 wherein the autoimmune disease is diabetes.

27. The method of Claim 26 wherein the autoimmune disease is viral-induced diabetes.